



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/527,156

03/09/2005

Masahiko Sisido

SAE-0031

1834

23353 7590 11/13/2007
RADER FISHMAN & GRAUER PLLC
LION BUILDING
1233 20TH STREET N.W., SUITE 501
WASHINGTON, DC 20036

EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

11/13/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,156	Applicant(s) SISIDO ET AL.	
	Examiner Dana Shin	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2007 and 21 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-15 and 17-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-15 and 17-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1635

DETAILED ACTION

Upon further consideration, new grounds of rejection are found to be applicable in the instant case. Examiner apologizes for any inconvenience caused by this Office action.

Status of Claims

Currently, claims 12-15 and 17-21 are pending. Claims 12, 14, 15, and 17 have been amended via examiner's amendment as appears on pages 2-3 of the Office action dated June 21, 2007.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Currently, none of the pending claims recites the steps of adding or introducing both a reaction initiator (e.g., a transesterification catalyst) and a reaction terminator (e.g., cPNA). As described in the specification, the reaction initiator as well as the reaction terminator are required to produce an aminoacyl-tRNA as claimed in the instant case. For instance, the specification teaches that the tRNA aminoacylation occurs when a transesterification catalyst (reaction initiator) is present in the reaction mix. See page 16. Further, the specification also teaches that the production of an aminoacyl-tRNA (final product) is made possible by terminating the

Art Unit: 1635

aminoacylation step by either increasing the reaction temperature (for ternary reaction) or adding a reaction terminator such as cPNA (for binary reaction). Since the claimed methods are drawn to both aminoacylating a tRNA and producing a final product of an aminoacyl-tRNA, it is concluded that both a reaction initiator and a reaction terminator are required in the claimed methods.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-15 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of aminoacylating a tRNA at its 3' hydroxyl group either by 1) a binary aminoacylation reaction wherein a tRNA is reacted with an antisense-amino acid PNA compound (aa-PNA) wherein the aa-PNA compound comprises two lysine amino acids attached to the carboxyl end of the aa-PNA and an amino acid to be transferred to the tRNA linked to the aa-PNA compound via an ester bond at the amino terminus, or 2) a ternary aminoacylation reaction, wherein a tRNA is reacted with a DNA template and an aa-PNA compound wherein the aa-PNA compound comprises two lysine amino acids attached to the carboxyl end of the aa-PNA and an amino acid to be transferred to the tRNA linked to the aa-PNA compound via an ester bond at the amino terminus and wherein the DNA template is complementary to the tRNA and the aa-PNA, wherein the method further comprises a reaction initiator and a reaction terminator

Art Unit: 1635

wherein the reaction initiator initiates transfer of the amino acid from the aa-PNA to the tRNA by transesterification thereby producing an aminoacyl-tRNA by terminating the aminoacylation; does not reasonably provide enablement for the full breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (*Wands*, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims are drawn to a method of aminoacylating a tRNA, thereby producing an aminoacyl-tRNA, wherein the method comprises an amino acid, antisense peptide nucleic acid, a cationic amino acid, an ester bond between the amino acid and the antisense peptide nucleic acid.

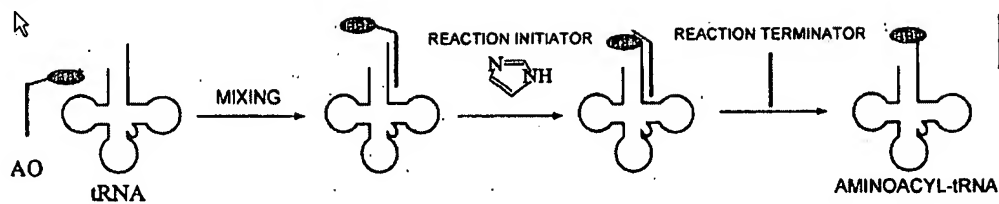
As applicant is aware, the claimed invention has been found to be free of the prior art. As such, the content of the specification and the amount of directions/guidance/working examples

provided by the inventor need to be sufficient for one of ordinary skill in the art to use the claimed invention as filed without undue experimentation. That is, the claimed invention must be commensurate in scope with the content or amount of the disclosure in the specification.

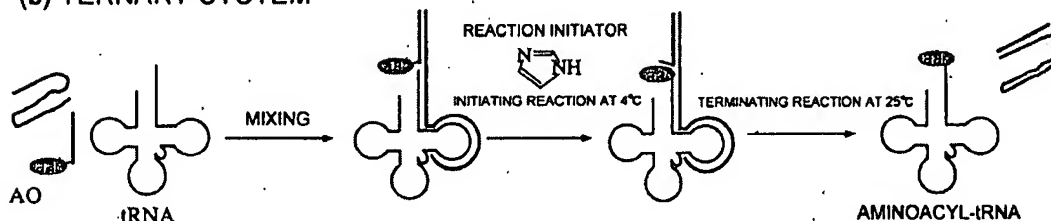
In the instant case, the claimed methods do not correspond in scope with the working examples and directions provided by the inventor, and therefore, one of ordinary skill in the art would not have been able to practice the entire scope of the claims without undue experimentation, especially because the nature of the invention, the state of the prior art, and the level of skill/predictability were nascent at the time of the invention.

As written, the claims do not recite required method steps for producing an aminoacyl-tRNA. The examples and the teachings of the specification suggest that one of ordinary skill in the art would not be able to produce an aminoacyl-tRNA without a reaction initiator (e.g., imidazole buffer or sodium phosphate) and a reaction terminator (e.g, cPNA or raising the reaction temperature to 25°C). See working examples wherein all reaction mixes contain either imidazole buffer or sodium phosphate for aminoacylation. As clearly depicted by the pictorial representation of the claimed aminoacylation methods (both binary and ternary systems) in Figure 2, both a reaction initiator and a reaction terminator are necessary in order to obtain an aminoacyl-tRNA as claimed and intended in the instant case. See below for Figure 2.

(a) BINARY SYSTEM



(b) TERNARY SYSTEM

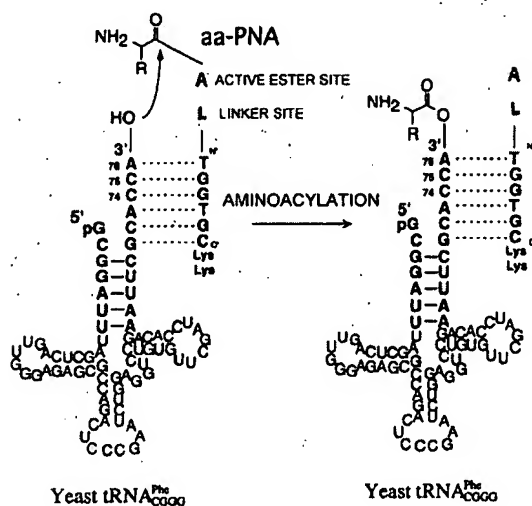


Further, the specification teaches that “by carrying out a transesterification reaction, the 3’ hydroxyl group is selectively aminoacylated.” See page 12. In other words, the transesterification reaction is a required method step to produce an aminoacyl-tRNA. The specification also teaches that the aminoacylation reaction is usually carried out in the presence of a transesterification catalyst such as imidazole. See page 16. In view of the foregoing, one of ordinary skill in the art would not have been able to produce an aminoacyl-tRNA without the help of a transesterification catalyst.

Moreover, the specification teaches that the amino acid residue that is to be introduced to a tRNA is not “introduced in the presence of an antisense molecule which is a peptide nucleic acid” as claimed in the instant case. In fact, the tRNA is mixed with a complex comprising an amino acid and an antisense PNA sequence, wherein the amino acid is attached to the antisense PNA sequence via an active ester/linker. That is, the claimed “amino acid to be introduced” is not reacted with the tRNA “in the presence” of an antisense PNA; rather, the aminoacylation

Art Unit: 1635

reaction is carried out by mixing a tRNA with a compound, which is named "aa-PNA" in the instant application. See Figure 4 below.

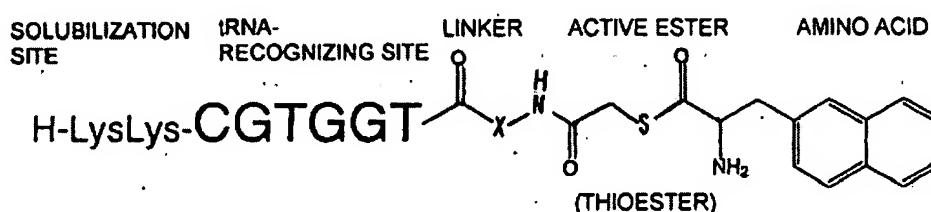


Further, there is no structural limitation for the antisense PNA (e.g., length limitation).

The broadest reasonable interpretation of the claim language, "an antisense molecule which is a peptide nucleic acid", embraces an antisense PNA of any length, such as 1000 nucleotides or 1 nucleotide. However, the specification teaches that the claimed aminoacylation method requires a certain length parameter for the antisense PNA to properly react with the tRNA. The specification states, "For a PNA, as a sequence binding to a tRNA, a sequence with a chain length of 4 to 10 is preferred (within a range of chain length which is easy to synthesize and whose binding to a tRNA is easy to control)." See page 13. The specification also states, "with regard to a PNA, there are problems that, when the chain length of a PNA becomes long, synthesis of the PNA is not easy, the control by temperature is difficult because its binding to a tRNA is too strong, and the like." See page 15. The specification also states, "as the PNA of an antisense molecule (AO), a sequence (with a chain length of 7 to 12) that binds to DNA but does not bind to a tRNA is preferred. When it is too long, it becomes difficult to dissociate the binding

by temperature because the binding to DNA is too strong. On the other hand, when it is too short, aminoacylation does not occur because the binding to DNA is too weak.” See page 16. As such, the length of the claimed antisense PNA is crucial for producing an aminoacyl-tRNA as claimed.

Further, it is unpredictable whether one of ordinary skill in the art would have been able to use the aminoacylation method without a compound of “formula (1)” that is represented as “H-cAm-PNA-L-E-Am” and expect to obtain an aminoacyl-tRNA as claimed in the instant case. Claim 17 was originally rejected under 35 U.S.C. 112, second paragraph for being indefinite because the symbol “H” was not described either in the claim or in the specification and therefore, one of ordinary skill in the art would not know the complete structure of the claimed “formula (1)”. In response to this rejection, applicant responded that the symbol “H” is understandable to one skilled in the art based on the drawings in Figure 1 and that “H” indicates -NH_2 located at the C-terminal of -cAm . See page 6 of the Remarks filed on April 9, 2007. Contrary to applicant’s assertion, the symbol “H” is not present or explained in Figure 1. Figure 3, however, shows the structure of the claimed “formula (1)” as below:



Perhaps, by combining Figure 1 and Figure 3, one might be able to extrapolate that the symbol “H” represents -NH_2 attached to the cationic amino acid. Provided that the claimed “formula (1)” is fully supported by the disclosure of the specification, one of ordinary skill in the art would not have been able to produce an aminoacyl-tRNA without using the claimed “formula (1)”, as evidenced by the specification, which teaches that the structure in Figure 3 is “an amino

[illegible]

See also page 15 of the specification, which teaches that the length of the DNA template should be “restricted to the length which is easy to control”.

Art Unit: 1635

Further, producing an aminoacyl-tRNA would not be feasible in the ternary aminoacylation method of claim 21 if the reaction was not terminated by a raised temperature to 25°C. See page 12 and Figure 2.

Since none of the claimed methods comprises all of the essential elements and steps required to produce an aminoacyl-tRNA as required by the claims, and since the specification clearly teaches that one of ordinary skill in the art needs all the essential elements and steps that are currently missing in the claims in order to use the claimed invention with a requisite effect, the claimed methods are not considered fully enabled.

In view of the totality of factors and reasons stated above, it is concluded that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

*/J. E. Angell/
Primary Examiner
Art Unit 1635*